Malaysia Stroke Conference 2022 Report and Stroke Update

Crystal Sing Chiek Teoh[1], Yik Hon Ho[2], Jie Ping Schee[3], Caryn Tsujean Lim[2], Irene Looi[4], Wan Asyraf Wan Zaidi[5], Fan Kee Hoo[6]

[1]Department of Medicine, Penang Hospital, Georgetown, Penang, Malaysia, [2]Department of Cardiology, Sarawak Heart Centre, Kota Samarahan, Sarawak, Malaysia, [3]Department of Medicine, Faculty of Medicine, University of Malaya**,** Kuala Lumpur, Malaysia, [4]Clinical Research Centre, Seberang Jaya Hospital, Perai, Penang, [5]Department of Medicine, Faculty of Medicine, Hospital Canselor Tuanku Muhriz, Universiti Kebangsaan Malaysia**,** Cheras, Malaysia, [6]Department of Medicine, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia**,** Serdang, Malaysia

BACKGROUND AND PURPOSE

Stroke is a leading source of disability and a major contributor to the disability-adjusted life years index. It is a needless impediment to sustainable social and economic growth. Because of the enormity of the burden of stroke globally, there is a real need to develop strategies to reduce its impact. With this in mind, the MSN Stroke Council together with the Malaysian Neuro-interventional Society, Malaysian Society of Geriatric Medicine and Malaysian Society of Rehabilitation Physicians have jointly organised this conference on stroke care in August 2022 with the theme of FAST: Brain and Heart Attack. Representatives from the Malaysian Society of Emergency Physicians, National Heart Association of Malaysia, and Family Medicine Association Malaysia were involved, together with other delegates from university hospitals, and Ministry of Health hospitals. Contributions from delegates allowed a broad set of principles to be put in place concerning stroke care that may be generalisable locally and regionally.

SUMMARY OF REPORTS

The Malaysia Stroke Conference was held from 12th to 14th August 2022, covering **a few key points** made in the areas of hyperacute and acute stroke, primary and secondary stroke prevention, stroke in geriatrics, rehabilitation, reorganisation of stroke network and bridging stroke care between district and tertiary hospital in Malaysia, rehabilitation, and role of Non-Government Organisation (NGO) i.e. Social Security Organisation (SOCSO) in stroke care.

CONCLUSION

This conference report provides a comprehensive review of the evidence regarding recent scientific and clinical advances in stroke and stroke systems of care to date. The consensus recommendations embodied in this report provides a framework for local and regional stroke service providers to establish minimum standards of stroke care and thus make a contribution toward reducing the global burden of stroke.

SCOPE AND PURPOSE

Malaysia Stroke Conference was an initiative of the Malaysia Stroke Council, Malaysian Neuro-interventional Society, Malaysian Society of Geriatric Medicine and Malaysian Society of Rehabilitation Physicians. To obtain a broad representation, delegates from the Malaysian Society of Emergency Physicians, the National Heart Association of Malaysia, Family Medicine Association Malaysia were involved, together with other delegates from university hospitals, the Ministry of Health hospitals were invited to contribute so that a broad set of principles could be put in place concerning stroke care, especially with continuous rise in the prevalence of diabetes, hyperlipidaemia, and obesity, ageing populations and ongoing Covid-19 pandemic. At the same time, regional variations in available resources for healthcare management, in general, could be taken into account. The general aims of the conference were to produce a series of statements with accompanying goals and specific interventions in the following areas: **(1) Hyperacute stroke (2) Acute stroke (3) Mechanical thrombectomy (4) Tandem occlusions (5) Tenecteplase in hyperacute stroke (6) Basilar stroke intervention (7) Intracerebral haemorrhage (8) Primary and Secondary stroke prevention (9) Stroke in geriatrics (10) Cerebrovascular disease and Neurocognitive disorders (11)Rehabilitation (12)Reorganisation of stroke network and bridging stroke care in Malaysia (13)The role of Social Security Organisation(SOSCO) in stroke care and (14) Telemedicine**

METHODS

The delegates were initially addressed by the following speakers at the opening ceremony: Associate Professor Dr Hoo Fan Kee (Chairperson of Malaysia Stroke Council & Malaysia Stroke Conference 2022) and Dr Sapiah Binti Sapuan (Head of Neurology Service). It was followed by the MSC 2022 Rising Star Award Ceremony which recognized the exceptional efforts of individuals who have contributed to the development and improvement of their respective stroke hospitals. Examples of works include: a) Initiation of stroke services b) Training of hospital stroke team c) Assisting the state stroke champions in stroke thrombolysis d) Stroke data collection and monitoring. The event continued with the announcement and handling of WSO Angels Award Winners to hospitals that exemplified excellent stroke care service.

The first part of the program consisted of a series of plenary sessions on various topics with regard to optimising thrombolysis and thrombectomy access in Malaysia, stroke in geriatric populations, addressing the critical interphase of critical intervention, the use of point of care ultrasound (POCUS) in stroke, evolution and challenges of stroke service in Covid-19 pandemic, the role of SOCSO in stroke care, post-stroke neurocognitive disorders and stroke rehabilitation. There were also symposiums discussing subjects on telestroke, the role of emergency medicine in hyperacute stroke, stroke prevention in atrial fibrillation, secondary stroke prevention, the role of antiplatelet therapy and Tenecteplase for acute ischemic stroke.

In the second part of the congress, stroke preceptor sessions were conducted in which issues related to diagnosis, imaging selection, inpatient investigations and

management, stroke mimickers, hospital workflow and trials related to stroke in extended hours and basilar stroke were addressed.

A draft of a consensus statement was presented to the group after which interactive discussion, modification of the statement, and/or complete replacement with a new statement were undertaken.

The consensus statements were reviewed by a broadly based consensus panel, the membership of which consisted of stroke neurologists, geriatricians, emergency and rehabilitation physicians and experts from SOCSO.

The following guidelines can be adopted according to the extent of resources in each state.

ABBREVIATIONS

Abbreviations	Meaning
ADAPT	Adoption of direct aspiration as first pass mechanical thrombectomy
AIS	Acute ischemic stroke
ASCVD	Atherosclerotic cardiovascular disease
ASU	Acute stroke unit
BP	Blood pressure
CI	Cognitive impairment
CMBs	Cerebral microbleeds
CRAO	Central retinal artery occlusion
CSC	Comprehensive stroke centre
CTA	CT angiography
DAPT	Dual antiplatelet therapy
ECG	Electrocardiogram
EVT	Endovascular thrombectomy
FBS	Fasting blood sugar
HbA1c	Haemoglobin A1C
HTRA 1	HtrA Serine Peptidase 1
IVT	Intravenous thrombolysis
ICA	Internal carotid artery
LDL	Low-density lipoprotein
LVO	Large vessel occlusion
MCA	Middle cerebral artery

MI	Myocardial infarction
MMSE	Mini Mental State Examination
MoCA	Montreal Cognitive Assessment
MT	Mechanical thrombectomy
MTHFR	Methylenetetrahydrofolate reductase
mTICI	modified Treatment In Cerebral Ischaemia
NIHSS	National Institutes of Health Stroke Scale
NASAM	National Stroke Association of Malaysia
NSTEMI/UA	Non-ST elevation myocardial infarction/ unstable angina
PSCI	Post stroke cognitive impairment
SAPT	Single antiplatelet
T2DM	Type 2 Diabetes Mellitus
TIA	Transient ischemic attack
VTE	Venous thromboembolism

PRIMARY PREVENTION

Reviewer: Fan Kee Hoo

Issues

1. Rising epidemic of vascular risk factors such as overweight/obesity, smoking, hypertension, diabetes and hypercholesterolaemia.

2. Challenges faced by Malaysia's primary care can be divided into system/providers factors (high patient load, time constraints, high staff turnover and shortages of well-trained staff, lack of continuity of care, lack of adherence to disease guidelines) and patients' factors (poor medication adherence, complex comorbidities, lack of self-management skills).

3. Navigating the future of healthcare in the era of digital health.

Goals

1. To construct and implement community-specific programs to identify and modify stroke risk factors, hence reducing the incidence of stroke and vascular dementia.

2. To encourage primary health care to be proactive in empowering patients and carers.

3. To enable patients to participate more in self-management by increasing their knowledge, skills and confidence and invite informed and shared decision-making.

4. To embrace the advances in digital health by introducing electronic health (e-Health) which enables the effective electronic exchange of health-related data between primary and tertiary care and ensures consistency in healthcare provision.

Specific interventions

1. Chronic Care Model was employed to improve health outcomes and quality of care in primary care settings. The 6 elements under this care model are:

a) Organisation of healthcare
b) Design of delivery system
c) Self-management support
d) Decision support
e) Clinical information systems
f) Community (providing informative resources and equitable policies)

2. Identify, treat, and monitor those with vascular risk factors at the primary care level. (Guidelines for the Primary Prevention of Stroke/ Malaysia CPG)

Elements	Recommendations
Physical activity	Moderate to vigorous-intensity aerobic physical activity at least 40 min per day for a minimum of 3 - 4 days per week is recommended to reduce the risk of stroke.
Diet	A diet with a reduced intake of sodium, and saturated fats, and emphasises on fruits, vegetables, and low-fat dairy products is recommended.
Hypertension	1. Regular BP screening, lifestyle modification and appropriate pharmacological therapy are recommended. 2. In the general population aged 60 years or older, initiate pharmacologic treatment to lower BP at a blood pressure of ≥ 150/90mmHg and treat to a goal SBP ≤ 150/90mmHg.
Cholesterol	1. Treatment with an HMG coenzyme-A reductase inhibitor

	(statin) medication is recommended for the primary prevention of ischemic stroke in patients. 2. Treatment with non-statin lipid-lowering therapies such as fibric acid derivatives, bile acid sequestrants, niacin, and ezetimibe may be considered in patients who cannot tolerate statins. 3. High-risk group: Aim LDL of <1.8 mmol/l (to tailor according to risk and CVSD); Intermediate and low risk: Aim LDL of <3.4mmol/l.
Diabetes mellitus	1. More intensive HbA1c glycaemic control targets (<6.5%) may be required for optimal ischemic stroke prevention. 2. Target BP for diabetics is <130mmHg systolic and <80mmHg diastolic, preferably <120mmHg if tolerated.
Obesity	Among overweight (BMI=25 to 29 kg/m2) and obese (BMI >30 kg/m2) individuals, weight reduction is recommended for reducing the risk of stroke.
Smoking	Smoking cessation is recommended due to the high correlation between smoking and both ischemic stroke and SAH.
Aspirin	Aspirin therapy is not recommended for primary prevention of stroke in the elderly, diabetics, or other high-risk groups.
Alcohol	1. Avoid alcohol or limit consumption of ≤ 2 drinks per day for men and ≤ 1 drink per day for non-pregnant women.

	2. Alcohol is best avoided, a recent publication revealed consumption of any amount of alcohol is associated with higher CVSD risk.
Public education	1. Educate the community about stroke, stroke symptoms, risk factors, primary and secondary prevention, and recovery. 2. Widespread education of patients and family members on healthy lifestyles, including smoking cessation, regular exercise, and reduction of obesity, cholesterol, excessive intake of salt, dietary fat, and alcohol, and other relevant risk factors.
Digital health	1. Utilisation of digital health apps (e.g. EMPOWER-SUSTAIN in Malaysia) in conjunction with support by healthcare providers to maximise its effectiveness in patients' self-management. 2. Develop user-friendly and effective e-health systems for rural people, and at the same time ensure security and privacy of the patients are properly maintained. 3. Establish more ICT infrastructure and make the internet available and affordable in rural areas.

HYPERACUTE STROKE

Reviewer: Sing Keat Wong

Goals

1. To increase stroke awareness among the public and health providers in differentiating stroke and stroke mimics.

2. Fast access to CT brain plain (stroke pathway with or without pre-hospital notification) to differentiate intracerebral haemorrhage from ischemic stroke, the consensus as per Ischemic Stroke Management Clinical Practice Guideline 2020, CT angiogram (Carotid to Circle of Willis) is recommended with or without prior advanced neuroimaging i.e. CT perfusion and MRI brain.

3. To provide acute stroke therapies as per evidence-based principles.

4. Administration of IVT in a timely, safe manner after considering indications/ contraindications and risks versus benefits.

5. To reduce the morbidity and mortality of acute stroke while increasing the proportion with minimal disability.

6. To provide rapid access (including emergency transport) for all patients with acute stroke to an acute stroke-ready hospital (district hospital) and, wherever possible, to primary or comprehensive stroke centres.

Recommendations

1. Adequate training to recognize stroke, good clinical examination skills and interpret hyperacute vascular imaging.

2. Device clear interhospital transfer workflows and protocols to facilitate the transfer of patients to stroke centres.

3. Intensify collaborative efforts and communications between the pre-hospital service team and the hospital's stroke team.

Timeline based eligibility criteria for thrombolysis (AHA)

Within 3 h - Age	For otherwise medically eligible patients ≥18 y of age, IV alteplase administration is equally recommended for patients ≤80 and >80 years of age.
Within 3 h - Severe stroke	IV alteplase is indicated within 3 h from symptom onset of ischemic stroke despite increased risk of hemorrhagic transformation.
Within 3-4.5 h - Mild disabling stroke	IV alteplase may be reasonable for patients who can be treated within 3 and 4.5 h of ischemic stroke onset or last known well.
3-4.5 h -Age	For patients >80 years old, IV alteplase is safe and can be as effective as in younger populations.
3-4.5 h - Early improvement in symptoms	IV alteplase is reasonable for patients who present with moderate-severe ischemic stroke and demonstrate early improvement but remain moderately impaired and potentially disabled in the judgement of the physician.
3-4.5 h - Pre-existing disability	For patients with preexisting disability (mRS score >=2), the decision to thrombolysis should take into account quality of life, social support, place of residence, need for a caregiver, patient's

	and family's preference and goals of care as they are associated with less neurological improvement and higher mortality.
3-4.5 h - Severe stroke	The benefit of IV alteplase for patients with very severe stroke symptoms (NIHSS score >25) is uncertain.
Wake-up and unknown time of onset	IV alteplase can be given if: a) DWI-FLAIR mismatch-presence of ischemic parenchymal brain lesion on MRI diffusion-weighted imaging but no corresponding hyperintensity on FLAIR (WAKE-UP Trial) b) Perfusion lesion-ischemic core mismatch – a ratio of >1.2 between the volume of hypoperfusion and the volume of the ischemic core with the absolute difference in volume >10mls and ischemic core volume of <70mls (EXTEND trial- 4.5-9 hours or wake up stroke).

Other indications

Extracranial cervical arterial dissection	IV alteplase in AIS known or suspected to be associated with extracranial cervical arterial dissection is reasonably safe within 4.5 hours and probably recommended.
Intracranial arterial dissection	IV alteplase benefits and bleeding risk in AIS known or suspected to be associated with intracranial arterial dissection remain unknown, uncertain and not well established.
Unruptured	For AIS patients who are known to harbour:

intracranial aneurysm	a) small or moderate-sized (<10mm) unruptured and unsecured intracranial aneurysm - Administration of IV alteplase is reasonable and probably recommended. b) giant unruptured, unsecured intracranial aneurysm- Benefits and risk of IV alteplase are not well established.
Cerebral microbleeds (CMBs)	In otherwise eligible patients who have CMBs demonstrated on MRI of: a) a small number (1-10) of CMBs - administration of IV alteplase is reasonable. b) high burden of CMBs (>10)- the benefits of IV alteplase are uncertain.
Extra-axial intracranial neoplasms	IV alteplase is probably recommended.
Acute MI	For patients presenting with concurrent AIS and acute MI, treatment with IV alteplase at the dose appropriate for cerebral ischemia, followed by percutaneous coronary angioplasty and stenting if indicated, is reasonable.
Recent MI	1. For AIS patients with a history of recent MI within the last 3 months, IV alteplase is reasonable in: i) NSTEMI/UA ii) STEMI involving the right or inferior myocardium; 2. IV alteplase may be reasonable for STEMI involving the left anterior myocardium.

Left atrial or ventricular thrombus	IV alteplase may be reasonable for patients with major AIS but it is of uncertain net benefit in patients with moderate AIS likely to produce mild disability.
Systemic malignancy with life expectancy > 6 months	IV alteplase may be beneficial provided there are no coagulation abnormalities, recent surgery or systemic bleeding.
Pregnancy	1. IV alteplase may be considered in pregnancy when the benefits of treating moderate-severe stroke outweigh the increased risks of uterine bleeding. 2. The safety and efficacy of IV alteplase in the early postpartum period (<14 days after delivery) have not been well established.
Vaginal bleeding	In the presence of recent or active vaginal bleeding causing clinically significant anaemia, emergency consultation with a gynaecologist is probably indicated before a decision on IV alteplase is made.
Stroke mimics	IV alteplase is probably preferred over delaying treatment to pursue additional diagnostic studies in stroke mimics.

MECHANICAL THROMBECTOMY (MT) FOR ACUTE ISCHEMIC STROKE

Reviwer: Hamidon Basri

Goals

1. Rapid acquisition of CTA in hyperacute settings to identify large vessel occlusion, assess collateral status to restore arrested blood flow in the affected vascular territory and salvage the ischemic brain tissue.

2. Successful recanalization as indicated by complete or greater than 50% filling of the distal branches in the expected territory (TICI 3), if achievable with reasonable safety.

3. Better understanding of vascular anatomy and clot composition.

4. Further improvements in the device and techniques used in thrombectomy.

Time and imaging based eligibility criteria for mechanical thrombectomy: Indications for thrombectomy in acute ischemic stroke from emergent large vessel occlusion (ELVO): report of the SNIS)

0-6 h from onset	1. Thrombectomy should be offered if CT / MRI DWI ASPECTS ≥ 6. 2. Thrombectomy may be reasonable for AIS patients with a large core infarct volume such as CT/MRI DWI ASPECTS < 6.
6-24 h from onset	1. Thrombectomy is recommended in selected patients with AIS who have LVO in the anterior circulation and meet advanced MRI DWI or CTP imaging criteria for DAWN or DEFUSE 3. 2. Thrombectomy may be considered in selected patients with anterior circulation AIS who do not meet imaging criteria for

	DAWN and DEFUSE 3 but otherwise have a 'favourable' imaging profile such as CT ASPECTS of 6–10, MRI DWI ASPECTS of 6–10, moderate-to-good collateral status on mCTA, or small (<70mL) core infarct on advanced MRI DWI-PWI or CTP imaging.

Location of LVO (Indications for thrombectomy in acute ischemic stroke from emergent large vessel occlusion (ELVO): report of the SNIS 2018)

Location	1. Thrombectomy is indicated in patients with occlusions of the ICA (including intracranial, cervical segments or tandem occlusion) and M1/M2 MCA. 2. The benefit of thrombectomy in more distal segments, such as MCA M3 or anterior cerebral artery is unclear and should be considered on a case-by-case basis.

Clinical profile

Stroke severity	1. Thrombectomy is indicated in patients with anterior circulation ELVO with an NIHSS score of ≥ 6. 2. Thrombectomy may be considered in patients with anterior circulation AIS and NIHSS score <6 when associated with disabling symptoms.

Age and baseline functional level

Age & baseline mRS score	1. Age >80 years should not be used as a contraindication for thrombectomy. 2. The benefit of thrombectomy in patients with baseline mRS score >1 is unknown.

MANAGEMENT OF TANDEM OCCLUSIONS IN ACUTE ISCHEMIC STROKE

Reviewer: Hamidon Basri

Endovascular Therapy of Anterior Circulation Tandem Occlusions / Management of tandem occlusions in acute ischemic stroke – intracranial versus extracranial first and extracranial stenting versus angioplasty alone: a systematic review and meta-analysis/ Tandem Lesions in Anterior Circulation Stroke Analysis of the German Stroke Registry–Endovascular Treatment

Introduction
Tandem occlusion involving concurrent occlusion of cervical ICA and intracranial large vessel occlusion (LVO) of either the intracranial ICA and/or proximal middle cerebral artery (MCA) showed poor response to IV thrombolysis alone. Recommendation: The treatment of cervical ICA during EVT is reasonable (level IIb evidence) and is associated with higher odds of favourable functional outcomes compared with medical therapy alone.
Intracranial versus Extracranial approach
It remains unclear if intracranial or extracranial lesions should be treated first. Treatment of the intracranial first approach resulted in reduced time to recanalization, whereas the extracranial first approach can improve collateralization while the intracranial thrombectomy is being performed. Recommendations:

No consensus exists regarding an extracranial first versus intracranial first approach up to date and no single approach can be advocated for consistently.

Extracranial stenting versus angioplasty approach

It remains unclear if extracranial lesions are best managed with stenting or angioplasty only at the time of initial treatment. The carotid stenting approach resulted in a definitive treatment at the time of the initial procedure but increases the risk of periprocedural haemorrhage as compared to angioplasty.

Recommendations:

1. Treatment of acute cervical ICA with stenting is associated with higher odds of successful reperfusion and favourable outcome compared with no cervical ICA stenting.

2. Aetiology of the cervical ICA lesion should be considered while planning EVT for acute ischemic stroke due to tandem occlusion as cervical ICA stenting was associated with favourable outcome in the atherosclerosis group but not in the dissection group.

3. Careful patient selection for cervical ICA stenting should be taken as stronger benefit is associated with lower NIHSS at admission.

4. It is important to weigh up the benefits of cervical ICA stenting against the potential risk of hemorrhagic complications from early antiplatelet agent administration, especially after intravenous thrombolysis. In fact, there was no difference in the rate of sICH and PH2 between the stent and no-stent groups; the better functional outcome was seen in the stent group.

5. Conservative treatment should be considered first in patients with dissection and cervical ICA stenting should be reserved for selected cases.

Antiplatelets management before and after emergent carotid artery stenting (CAS) for extra-cranial internal carotid artery (EC-ICA) occlusion in the setting of acute ischemic stroke

Before CAS	(Antiplatelet Therapy During Emergent Extracranial Internal Carotid Artery Stenting: Comparison of Three Intravenous Antiplatelet Perioperative Strategies) / Antiplatelet Therapy During Emergent Extracranial Internal Carotid Artery Stenting: Comparison of Three Intravenous Antiplatelet Perioperative Strategies 1. No specific recommendation exists with respect to the antiplatelet regimen for EC-ICA emergent stenting, due to the lack of direct comparison between different antiplatelet strategies. 2. In the acute phase administration of IV aspirin, if available, or IV glycoprotein IIb/IIIa receptor antagonist, such as abciximab, would be possible. 3. However, the ideal medical regimen in CAS for acute stroke is not known, and it must be borne in mind that aggressive anticoagulation, especially in combination with thrombolytics, may increase the risk of ICH. 3. Examples of intravenous antiplatelets used: aspirin, clopidogrel, Eptifibatide, tirofiban, Abciximab, Cangrelor.
After CAS	post stenting: Postprocedural Antiplatelet Treatment after

	Emergent Carotid Stenting in Tandem Lesions Stroke / Mechanical thrombectomy in tandem occlusion: procedural considerations and clinical results / Dual antiplatelet therapy after carotid artery stenting: trends and outcomes in a large national database 1. After emergency stent implantation, antiplatelet medication is necessary to prevent acute stent thrombosis. 2. Secondary prophylaxis with DAPT daily is superior to aspirin monotherapy or aspirin plus heparin. 3. A multi-speciality consensus statement recommends at least 4 weeks of post-CAS dAPT followed by lifelong treatment with SAPT. 4. In Malaysia settings, DAPT (aspirin-clopidogrel) is for 3 months, then SAPT (aspirin/clopidogrel) lifelong is practised. 5. However, the potential benefit of prolonging DAPT concerning ischemic complications must be balanced with the corresponding increased risk of haemorrhage.

Technique European Stroke Organisation (ESO)- European Society for Minimally Invasive Neurological Therapy (ESMINT) guidelines on mechanical thrombectomy in acute ischemic stroke

Statements	Evidence/Suggestions
Comparison of MT using direct aspiration compared with a stent	1. There is currently no evidence that contact aspiration alone improves

retriever for adults with LVO related acute ischemic stroke	functional outcomes compared with BMM in patients undergoing MT. 2. There is currently no evidence that contact aspiration alone increases the rate of reperfusion over thrombectomy using a stent retriever. 3. Stent retriever is preferred as compared to contact aspiration alone for MT in patients with acute ischemic stroke. 4. ADAPT may be used as standard first line treatment, followed by stent retriever thrombectomy as rescue therapy if needed.

Conclusions

1. Mechanical thrombectomy for anterior circulation stroke due to proven proximal LAO within 6 hours of stroke onset is safe and highly effective.

2. The overall rate of independent functional outcome (mRS 0-2) at 90 days is about 20% greater with MT than with best medical therapy alone (which in most cases included IVT), and about half of the patients achieve very good outcomes after MT.

3. Favourable outcomes from MT in most patients are strongly time-dependent ('time is brain'), and best results are achieved when an early ischaemic brain injury is limited (for example, ASPECTS score ≥ 5).

4. If good recanalisation is achieved within 4.5 hours, the absolute rate of good

functional outcome exceeds 60%.

5. MT is highly likely to be cost-effective or even cost-dominant over a lifetime analysis.

TENECTEPLASE (TNK) IN HYPERACUTE STROKE

Reviewer: Zhe Kang Law

1. TNK is more fibrin specific, with a longer half-life of more than > 90-130 minutes, better reperfusion rate, lesser bleeding rates and easier to administer (single bolus in 5 seconds).

2. The optimal dose of TNK is 0.25m/kg. At this dose, it has a similar safety profile and is non-inferior in efficacy compared to Alteplase.

3. TNK reduces time from imaging to thrombolysis by 9 minutes; in CSC settings by 12 minutes; in drip-and-ship settings, Tenecteplase reduces IVT to puncture time by 11 minutes and improves functional dependence (TETRIS registry).

4. TNK is more cost-effective than alteplase.

Indications	Recommendations
TNK in standard time window (4.5 hours from definite onset)	TNK is an alternative to alteplase for all patients presenting with acute ischaemic stroke who meet standard criteria for thrombolysis. AcT trial which compared Tenecteplase 0.25mg/kg vs Alteplase 0.9mg/kg showed non-inferiority in primary outcome defined as mRS 0-1 at 90-120 days.
TNK for wake-up stroke/unsure onset stroke/ extended time window stroke	The benefits of TNK beyond the standard time window are uncertain. Several trials are ongoing to supplement data in its use < 4.5 hours and between 4.5-24 hours. TWIST trial which compared Tenecteplase 0.25mg/kg versus no IVT use in less than 4.5 hours from wake up, NIHSS ≥ 3 or aphasia,

	using only non-contrasted CT assessment, showed that tenecteplase did not improve outcome. The current consensus did not support TNK utilisation in this group.
TNK in minor stroke	TNK is a reasonable alternative for minor strokes. NOR-TEST trial compared Tenecteplase 0.4mg/kg vs Alteplase 0.9mg/kg showed TNK was not superior to alteplase in improving functional outcome. However, taking into account results from other trials (including NORTEST-2A which showed harm of TNK at 0.4mg/kg), the recommended dose for TNK is 0.25mg/kg with a max of 25mg. TNK at a dose of 0.4mg/kg is not recommended.
TNK in LVO (Please refer CPG Management of Ischemic Stroke 3rd edition)	Tenecteplase is superior as bridging therapy when given ≤ 4.5 hours. EXTEND-IA TNK which compared Tenecteplase 0.25mg/kg vs alteplase before thrombectomy showed superiority of Tenecteplase with a reperfusion rate of 22% vs 10% and better functional outcome in patients with LVO.
TNK in BAO	TNK may be associated with an increased rate of reperfusion in comparison with alteplase before EVT in BAO. Randomised controlled trials to compare TNK with alteplase in patients with BAO are warranted. (Pooled analysis of BATMAN registry and EXTEND-IA TNK demonstrated a reperfusion rate of 26% vs 7% in Alteplase with no effect on the functional outcome). In the setting of clear onset stroke

	within 4.5 hours from the onset, TNK 0.25mg/kg maximum dose of 25mg may be considered as a reperfusion lytic treatment.
TNK in elderly	Tenecteplase 0.25 mg/kg given before endovascular therapy in patients >80 years old with large vessel occlusion stroke is associated with better functional outcomes at 90 days and reduced mortality when compared to tenecteplase 0.40 mg/kg or alteplase 0.90 mg/kg. (Class II evidence-EXTEND-IA pooled analysis).

1 vial of Tenecteplase (50mg)

Body weight	Dose (0.25mg/kg)	TNK dilution 10mls = 50mg
<60 kg	15.0 mg	3.0mls
60-70 kg	17.5 mg	3.5mls
70-80 kg 80-90 kg	20.0 mg 22.5mg	4.0mls 4.5mls
>90 kg	25mg.	5mls

*clinician should realise that the max dose of TNK in ischaemic stroke is 25mg,

therefore only half the vial of a 50mg TNK vial will be used.

BASILAR STROKE

Reviwer: Presaad Pillai

Issues

1. BASICS (2021) and BEST (2020) endovascular trials showed directional benefit in the primary outcome (mRS≤3 at 90 days) between endovascular treatment (EVT) versus best medical management (BMM) for basilar artery occlusion (BAO), however, it did not reach statistical significance. Symptomatic intracranial haemorrhage rates and mortality were comparable between the 2 treatment groups in both trials.

Latest updates

1. ATTENTION and BAOCHE trials which were published in 2022 showed overwhelmingly positive results favouring EVT in BAO.

2. ATTENTION recruited patients presenting within 12 hours of stroke onset whereas BAOCHE enrolled patients presenting within the 6 to 24-hour time window.

3. In terms of the primary outcome, a good functional outcome which was defined as mRS 0-3 at 90 days in both trials, was achieved by 46% of patients in the intervention group versus 23% in the control group (adjusted rate ratio, 2.06; 95% confidence interval [CI], 1.46 to 2.91, P<0.001) in ATTENTION. BAOCHE demonstrated 46% good functional outcome in the intervention group compared to 24.3% in the control group (adjusted rate ratio, 1.81; 95% confidence interval [CI], 1.26 to 2.60; P<0.001).

4. ATTENTION showed a significant reduction in 90-day mortality rates in the thrombectomy group compared to the control (37% vs 55%, adjusted risk ratio, 0.66; 95% CI, 0.52 to 0.82) despite increased symptomatic intracranial haemorrhage (sICH) in the thrombectomy group (6% vs 0%). BAOCHE showed similar trends of increased

sICH and reduced 90-day mortality in the thrombectomy group however the reduction in 90-day mortality in the thrombectomy group compared to the control (31% vs 42%) did not reach statistical significance (adjusted risk ratio, 0.75; 95% CI, 0.54 to 1.04).

5. In the ordinal shift of mRS, the adjusted common odds ratio (aCOR) towards better outcomes with thrombectomy was 2.87 in the ATTENTION and 2.64 in BAOCHE. This was comparable to anterior circulation thrombectomy trials with aCOR of 2.49 in HERMES and 2.54 in AURORA for ordinal mRS shift for a better outcome.

Conclusion

1. ATTENTION and BAOCHE have demonstrated that EVT is the standard of care for patients with basilar artery occlusions presenting either in the early or late time window and these findings are comparable to anterior circulation trials.

2. EVT in BAO has higher rates of good functional outcome and overall ordinal shift in mRS as well as lower 90-day mortality rates despite an expected increase in sICH.

3. ATTENTION and BAOCHE trials were restricted to Han Chinese patients who had a higher rate of intracranial arterial atherosclerosis which then required more intracranial stenting. Therefore, we can assume that patient populations with lower rates of atherosclerosis disease may benefit more from EVT.

Areas of improvement/ research interest

1. Application of the latest evidence-based medicine with adjustment to Malaysia's local settings in the management of acute BAO.

2. To strive for robust multicenter registries with well-maintained records of both cases and controls so that large sample registries of worldwide calibre can be rapidly acquired for analysis.

ACUTE STROKE CARE (24HOURS-7DAYS)

Reviwer: Jiann Shayng Tay

Goals

1. Early acute stroke care (first 24-48 hours) is pertinent to prevent early neurological deterioration, optimise cerebral perfusion, maximise functional recovery, monitor for early complications and prevent recurrent events.
2. Setting up effective acute stroke units which allow a more accurate diagnosis to be reached, more appropriate investigation to be carried out, prevention of secondary complications, earlier intensive rehabilitation and individualised patient care.
3. Inpatient investigations should aim to discover the mechanisms of current stroke as the effectiveness of stroke prevention is closely related to the stroke mechanism.
4. Good history and physical examinations to guide inpatient investigations.
5. Effective, supported discharge plan to prevent recurrence of stroke.

Specific interventions

Post IVT patients ideally should be managed in the Acute Stroke Unit (ASU).

Care aspects	Rationale
Managing team	1. An organised inpatient stroke unit care was characterised by a multidisciplinary team consisting of staff with a special interest in stroke ± rehabilitation, routine involvement of carers in the rehabilitation process in addition to the regular running of education and training programmes for staff. 2. ASU should aim to provide standardised assessment, early

	management protocol and early active rehabilitation for every inpatient.
NIHSS monitoring	1. For IVT patients, it is recommended to have intensive NIHSS monitoring (q 15 min for 2 hours, q 30 min for 6 hours and hourly for 16 hours). 2. For non-IVT patients, less intensive NIHSS monitoring is required, however, care should be taken if NIHSS increase by 4 points from baseline.
BP	1. For IVT patients, a strict BP target is reasonable (<180/105mmHg) but no lower than 130-140mmHg for the first 72 hours. 2. For non-IVT patients, permissible hypertension is reasonable for the first 24-48 hours (< 220/120mmHg).
Blood glucose	Aim to achieve blood glucose levels in the range of 140-180mg/dl (7.8-10mmol/l) and avoid blood glucose < 60mg/dl (3.3mmol/l) during the first 24 hours after AIS.
VTE prophylaxis	1. Intermittent pneumatic compression is an effective and inexpensive method. 2. Anticoagulation with unfractionated heparin (UFH) or low molecular weight heparin (LMWH) or heparinoid should be considered if the benefits outweigh the risks. 3. Maintain adequate hydration 4. Aim for early mobilisation.

Swallowing assessment	A bedside water swallowing test is a useful screening test and will dictate the need for a formal swallowing assessment referral.
Brain imaging	1. Emergent CT scan and discontinuation of alteplase infusion are warranted if the patient develops a severe headache, acute hypertension, nausea, or vomiting or has a worsening neurological examination. 2. CT or MRI scan 24 hours after IV alteplase should be obtained before starting anticoagulants or antiplatelet agents.
Others	1. Adequate hydration to maintain cerebral perfusion. 2. Delay placement of nasogastric tubes, indwelling bladder catheters, or intra-arterial pressure catheters if the patient can be safely managed without them (at least after 24 hours).
Management of post stroke complications	Infection, pressure sores, delirium, and post-stroke depression

Evaluations of AIS patients to prevent recurrent stroke: (AHA/ASA)

Investigations	Justifications
Brain Imaging	MRI is reasonable to guide the selection of secondary stroke prevention treatments in conditions: a) patients with carotid stenosis who are potential candidates for carotid revascularization in whom NCCT does not allow accurate

	localization. b) patients with PFO who are potential candidates for mechanical closure. c) patients with ischemic stroke and a treatment plan that includes anticoagulants to assess for haemorrhagic transformation and final infarct size.
Vascular imaging	MRA/CTA neck/brain to screen for: a) stenosis in patients with symptomatic anterior circulation cerebral infarction /TIA who are candidates for revascularization b) arterial dissection c) moya-moya or other vasculopathies
Transcranial Doppler (TCD)	TCD with embolus detection might be reasonable to screen for right-to-left shunt in ischemic stroke/TIA patients contemplating PFO closure.
Cardiac evaluation	1. In patients with acute ischemic stroke/TIA and without previously known AF, monitoring for AF is recommended using a short-term ECG recording for at least the first 24 hours, followed by continuous ECG monitoring for at least 72 hours whenever possible. 2. In patients with cryptogenic stroke, long-term rhythm monitoring with mobile cardiac outpatient telemetry or implantable loop recorder is reasonable to detect paroxysmal AF. 3. Transthoracic Echocardiography (TTE) is useful to diagnose

	PFO, intracardiac thrombus, myxoma, and endocarditis for all stroke patients. 4. Transesophageal echo (TOE) with Valsalva manoeuvre on agitated Gelofusin microbubble test +/- transcranial doppler is the gold standard to confirm PFO.
Vascular risk factors identifications	Complete blood count, coagulation profile, creatinine, fasting plasma glucose, HbA1c, fasting lipid profile are recommended to assess risk factors for stroke.
Thrombophilia screen	Testing for inherited thrombophilia in young stroke is of questionable clinical utility. The diagnostic yield is probably highest among young adults with cryptogenic stroke, prior miscarriages or thrombosis during pregnancy, and personal or family history of venous thrombosis.
Antiphospholipid screen	Routine testing is not recommended for patients with ischemic stroke who have no other manifestations of the antiphospholipid syndrome and who have an alternative explanation for their ischemic event such as atherosclerosis, carotid stenosis, or atrial fibrillation.
Hyperhomocystein -emia	Routine screening for hyperhomocysteinemia among patients with a recent ischemic stroke is not indicated.
Genetic testing (Notch 3/HTRA	Reasonable to be performed in patients with cryptogenic stroke.

1/MTHFR 677C-T gene)	
Vasculitis panel, markers of systemic inflammation	Reasonable to be performed in patients with cryptogenic stroke to diagnose CNS vasculitis.
Biohazard and drugs screen (cocaine/amphetam-ines)	Reasonable to be performed in patients with cryptogenic stroke.

INTRACEREBRAL HAEMORRHAGE (ICH)

Reviewer: Zhe Kang Law

Introduction

Hematoma expansion is devastating. TICH-2 studies showed that it is associated with worse outcomes in terms of mRS shift analysis OR 2.49 ($p<0.0001$), death at day 7 OR 5.99 ($p< 0.0001$), death at day 90 OR 2.58 ($p < 0.0001$), length of stay OR 0.72 ($p < 0.0001$) and also worse cognition, mood and quality of life scores.

Specific interventions (2022 AHA/ASA guidelines for management of patients with spontaneous intracerebral haemorrhage)

Recommendations	Justifications
Blood pressure control	1. Blood pressure lowering within 2 hours of ICH onset and aim to reach the target within 1 hour. 2. Mild-moderate ICH with presenting SBP 150-220 mmHg, acute lowering of SBP to a target of 140 mmHg to maintain between 130-150 mmHg is reasonable. Acute lowering of SBP to < 130mmHg is potentially harmful. 3. Large-severe ICH or those requiring surgical decompression, the safety and efficacy of intensive BP lowering are not well established.
Patients on antiplatelet therapy	1. Consider platelet transfusion for patients with spontaneous ICH on antiplatelet(aspirin) who need emergent neurosurgery interventions. Platelet transfusions

	are potentially harmful and should not be administered if no neurosurgery interventions are needed. 2. The effectiveness of desmopressin with or without platelet transfusions to reduce hematoma expansion in patients with spontaneous ICH being treated with antiplatelet is uncertain.
Patients on Vitamin K antagonists (warfarin)	1. ICH and INR > 2: PCC is preferred over FFP. 2. ICH and INR 1.3-1.9: PCC is reasonable. 3. Intravenous Vitamin K should be given after the replacement of the coagulation factor (PCC or others) to prevent an increase in INR later.
Patients on UFH or LMWH	Intravenous protamine is reasonable.
Patients on other anticoagulants eg Rivaroxaban, Dabigatran, Apixaban	1. Direct FXa inhibitors: Andexanet alpha as the reversal, PCC may be considered. 2. Dabigatran: Idarucizumab as the reversal, PCC may be considered.

Recommendations for General Hemostatic Treatments

1. The effectiveness of recombinant factor VIIa to improve functional outcomes in patients with spontaneous ICH (with or without the spot sign) is unclear.

2. The effectiveness of tranexamic acid in improving the functional outcome of patients with spontaneous ICH (with or without the spot sign, black hole sign or blend sign) is

not well established.

SECONDARY STROKE PREVENTION

Reviewers: Wan Chung Law, Abdul Hanif Khan Yusof Khan

Goals

1. Early initiation of treatment (within 24 hours) after TIA/minor stroke to advert the risk of early stroke recurrence. (EXPRESS study)
2. Multimodal treatment involves anti-thrombotic (SAPT/DAPT/OAC), blood pressure control, cholesterol-lowering drug, diabetic control, in addition to exercise and lifestyle changes is crucial.

Specific interventions (AHA/ASA)

Components	Recommendations
Hypertension	1. A BP goal of <130/80 mm Hg is recommended for most patients to reduce the risk of recurrent stroke and vascular events. A higher threshold may be justified in the frail/ elderly/limited life expectancy populations. 2. Antihypertensive treatment with a thiazide diuretic, angiotensin-converting enzyme inhibitor, or angiotensin II receptor blocker is useful for lowering BP and reducing recurrent stroke risk.
Hyperlipidemia	1. Lipid-lowering therapy with a statin and also ezetimibe, if needed, to attain an LDL-C of 1.8mmol/L (<70 mg/dL) is recommended to reduce the risk of major cardiovascular events in patients with ischemic stroke or TIA and atherosclerotic disease (intracranial, carotid, aortic, or coronary). 2. PCSK9 (proprotein convertase subtilisin/kexin type 9) inhibitor can be considered for patients with ischemic stroke who still have an LDL-C >

	1.8 mmol/L (>70 mg/dL) despite taking maximally tolerated statin and ezetimibe therapy who have a very high risk to prevent ASCVD events.
Glucose	A goal of HbA1c ≤7% is recommended for most diabetic patients with an ischemic stroke/TIA, especially those <65years old and without life-limiting comorbidities to reduce risk for microvascular complications.
Non-cardioembolic stroke	1. Single antiplatelet (SAPT) is indicated for secondary stroke prevention in most patients with non-cardioembolic ischemic stroke or TIA. 2. In patients presenting minor non-cardioembolic stroke (NIHSS ≤ 3) or high-risk TIA (ABCD ≥ 4) who did not receive IV alteplase, treatment with dual antiplatelet (DAPT) started within 24 hours of symptoms onset and continued for 21 days is effective in reducing the risk of recurrent ischemic stroke for a period of up to 90 days from symptom onset. 3. Cilostazol may be an alternative for patients with diffuse fragile small vessel disease and therefore at a higher risk of cerebral haemorrhage. (PICASSO, CSPS 2 trial) 4. Ticagrelor might be preferred to clopidogrel for secondary stroke prevention for patients with minor ischemic stroke or TIA who were carriers of CYP2C19 loss -of -function alleles. (Ticagrelor versus Clopidogrel in CYP2C19 loss-of-function Carriers with Stroke or TIA. N Engl J Med. 2021 Dec 30;385(27):2520-2530. doi: 10.1056/NEJMoa2111749. Epub 2021 Oct 28. PMID: 34708996.)
Atrial fibrillation and antithrombotics	1. In AF patients with an ischemic stroke/TIA, long term secondary prevention of stroke using OAC is recommended if there is no strict

	contraindication to OAC use, with a preference for NOACs over VKAs in NOAC-eligible patients. 2. HAS-BLED score has no bearing on the indication or contraindication of prescribing oral anticoagulants (OAC). It served as a reminder to practitioners to be judicious of the bleeding events. 3. Adequate dosing of NOAC can reduce the risk of stroke/systemic embolism, hospitalisation and death without a significant increase in major bleeding risk. 4. Algorithm for breakthrough ischemic stroke in patients while on OAC: a) rule out non-adherence b) rule out competing mechanisms c) rule out thrombus in the left atrial appendage (LAA) and to consider LAA occlusion if present d) if there is no thrombus in LAA, switching to a DOAC with a different mechanism might be reasonable in addition to investigate for other vascular risk factors. 5. The timing of initiation of anticoagulation for non-bleeding stroke as per is at 1-3-6-12 days after TIA, mild (NIHSS <8), moderate (NIHSS 8-16) and severe stroke (NIHSS >16). 6. For bleeding stroke (for example hemorrhagic transformation with concurrent multifocal infarcts and multiple vascular risk factors or cerebral microbleeds /cerebral amyloid angiopathy), the timing of initiation of OACs is case-by-case basis and decision should be guided by repeat CT brain and advanced vascular imaging (MRI/MRA/Circle of Willis). 7. A strict BP aim of < 120/80mmHg is recommended before initiation of OAC.

Cardiomyopathy	1. In patients with ischemic stroke /TIA and left atrial appendage thrombus with concomitant cardiomyopathy (ischaemic, non-ischaemic, or restrictive) and LV dysfunction, anticoagulant therapy with warfarin is recommended for at least 3 months to reduce the risk of recurrent stroke or TIA. 2. In patients with ischemic stroke or TIA in sinus rhythm with ischaemic or non-ischaemic cardiomyopathy and reduced EF without evidence of left atrial or LV thrombus, the effectiveness of anticoagulation compared with antiplatelet therapy is uncertain. 3, In patients with stroke or TIA and new LV thrombus (<3 months), the safety of direct oral anticoagulants to reduce the risk of recurrent stroke is uncertain.
Extracranial large artery atherosclerosis (ESC 2017)	1. CEA is recommended in patients with symptomatic 70-99% carotid stenoses. 2. CEA should be considered in patients with symptomatic 50-69% carotid stenoses. 3. Revascularization of 50-99% stenoses performed within 14 days after the index event is reasonable. 4. CAS should be considered for patients with symptomatic 50-99% carotid stenoses that are at high risk for CEA (adverse anatomical features or medical comorbidities).
Intracranial large artery atherosclerosis	1. In patients with an ischemic stroke or TIA due to 50-99% stenosis of a major intracranial artery, aspirin is preferred compared to oral anticoagulation. (WASID)

(ESO ICAD 2022/AAN stroke prevention in symp ICAD 2022)	2. In patients with an ischemic stroke or TIA due to severe stenosis (70-99%) of a major intracranial artery, dual antiplatelet therapy with aspirin and clopidogrel for a treatment duration of up to 90 days is reasonable. (SAMPRISS) 3. High-intensity statin therapy to achieve a goal of LDL < 1.8 mmol/L (<70 mg/dL), long-term BP target of <140/ 90 mm Hg in clinically stable patients with sICAS, moderate physical activity, and treatment of other modifiable vascular risk factors are recommended to reduce the risk of recurrent stroke and vascular events. 4. In patients with a stroke/TIA due to moderate stenosis (50-69%)of a major intracranial artery, angioplasty or stenting is associated with higher peri-procedural risk and is thus, not recommended. 5. In patients with severe stenosis (70-99%) of a major intracranial artery, endovascular therapy with intracranial angioplasty and or stenting is not recommended as a treatment of first choice.
Covert cerebral small vessel disease (ccSVD) (ESO ccSVD 2021)	1. Use of antihypertensive therapy in ccSVD patients with hypertension (BP >= 140/90 mmHg) is recommended. 2. Lipid-lowering with a statin can be considered in ccSVD patients at high risk of vascular events as primary prevention. 3. Healthy lifestyle interventions are recommended as primary prevention for vascular events. 4. Use of glucose-lowering therapies in diabetic patients who may have ccSVD is recommended. However, this treatment is not recommended in non-diabetic patients.

	5. Use of antiplatelet therapy in ccSVD patients with no other indications for this treatment and use of antidementia drugs are not recommended.
Patent foramen ovale (PFO) (ASA 2021)	1. In patients with a non-lacunar ischemic stroke of undetermined cause despite a thorough evaluation and a PFO with high-risk anatomic features, it is reasonable to pursue PFO closure over antiplatelet therapy alone for preventing recurrent stroke. 2. In patients with ischemic stroke with concomitant presence of ASD and PFO, closure of both anatomical defects is recommended. 3. In patients with a non-lacunar ischemic stroke of undetermined cause and a PFO, the decision for PFO closure versus medical management should be made jointly by the patient, cardiologist, and neurologist.
Embolic stroke if uncertain source (ESUS) (ASA 2021)	For embolic strokes of an undetermined source (ESUS), it is recommended to give SAPT. OAC and ticagrelor have not shown benefits based on the latest studies.
Lifestyle modifications	1. Smoking cessation 2. Increase physical activity 3. Weight loss 4. Diet which limits food high in saturated fat/cholesterol, sweetened food and red, processed meats 5. Diet which emphasises consumption of more fruits, vegetables, legumes, whole grains and fat-free/low-fat dairy

STROKE IN GERIATRIC POPULATIONS

Reviewer: Wee Koi Cheah

Goals

1. To recognize that stroke could present differently in the elderly.

2. To improve functional outcomes and reduce stroke-related complications in elderly patients.

3. To redefine the treatment of stroke in elderly patients.

4. Seamless stroke care for elderly patients in the community

5. To acknowledge the importance of advanced care planning in post-stroke elderly patients.

Issues

1. Non-specific symptoms such as delirium, falls, numbness, speech and visual disturbance, and unusual pain /headache, as atypical presentations of stroke in the elderly.

2. Late stroke presentation occurred frequently in the elderly due to numerous reasons such as assuming symptoms are part of ageing, having low expectancy for good health, better symptom tolerability and fear of seeking medical attention.

3. Geriatric patients were often excluded or under-represented in studies of acute stroke treatment-related complications and treatment efficacy (either IVT or mechanical thrombectomy or both).

4. Stroke prevention in the elderly is complex not only because there is not many randomised controlled trials (RCTs) involving this age group that can provide treatment evidence, but also because the stroke etiologies changes with ageing and there is a large

body of evidence from geriatric medicine that potentially conflicts with usual stroke preventative measures (eg data on frailty, polypharmacy, and falls)

5. The elderly post-stroke patients are more likely to develop post-stroke complications i.e. physical and cognitive impairment, urinary or faecal incontinence, bone fractures, infection, joint contractures, pressure sores and psychological disturbances.

6. Rehabilitation efforts as part of post-stroke care in elderly patients are often inadequate or started late.

7. Barriers to establishing an integrated multidisciplinary approach in elderly care are namely limited trained personnel, lack of continuity of care and lack of medications at community hospitals and clinics.

8. Advanced care planning is not often discussed as part of stroke care in Malaysia. Decisions on life-prolonging treatment are often made more difficult with communication difficulties, cognitive impairment and challenges with prognostication.

Specific interventions

Interventions	Rationale
Acute stroke therapy	IVT and/or EVT should become the standard of care for geriatric patients as well. However, careful selection of eligible patients especially for mechanical thrombectomy by routine assessment of pre-stroke frailty may help with the decision-making.
Primary prevention	Treatment of hypertension, antithrombotic for AF, statin, and healthy lifestyles.

Secondary prevention	1. Ischemic stroke: Blood pressure and cholesterol-lowering, antithrombotic for AF, carotid intervention and healthy lifestyle 2. Hemorrhagic stroke: Blood pressure lowering, avoiding antithrombotic, healthy lifestyle
Elderly post-stroke care	Components involved: 1. Identification and management of post-stroke cognitive impairment 2. Recognition and management of bladder/bowel dysfunction 3. Identification and management of post-stroke bone fragility 4. Fall prevention and exercise 5. Prevention of post-stroke infection, pressure sores and deep vein thrombosis (DVT) 6. Pain and fatigue management 7. Early supported discharge services which include home visits, family meetings and out-of-hospital rehabilitation 8. Financial and societal support via non-government organisations (NGOs), private agencies and social welfare.
Stroke rehabilitation	Stroke rehabilitation should be commenced as soon as patients are medically stable, however, individualised clinical judgments are indicated in older patients and patients with intracerebral haemorrhage.

Medication review	Identify drugs that are no lower indicated, appropriate or align with goals of care. Examples of validated tools that can be used are Beers Criteria 2019 (American), STOPP (European), STOPP-Frail, and STOPP-Fall.
Advanced care planning	1. The discussion of advanced care planning needs to be established early at the diagnosis of stroke. 2. It should aim to ascertain patients' wishes and preferences, communicate with them about the prognostic uncertainty, and engage carers throughout the process to remove any cognitive biases. 3. An in-hospital Clinical Ethics Committee should be established to help to resolve certain conflicts of decision-making on advanced care planning for patients.
Family/carer involvement	Family and carers should be actively involved in the whole continuum of stroke care. For example, a shared decision between patient, family and health care providers is fundamental in ensuring the success of deprescribing and in setting realistic goals of care.

CEREBROVASCULAR DISEASE AND NEUROCOGNITIVE DISORDERS

Reviewer: Kit Mun Tan

Issues

1. Early onset post-stroke dementia (PSD) results from a complex interplay between stroke lesion features and brain resilience. Chronic brain damage including WMH, MTLA and Alzheimer's disease pathology seen on magnetic resonance imaging (MRI) are associated with incident dementia after stroke/TIA.

2. Delayed-onset PSD is associated mainly with the presence of severe sporadic small vessel disease (WMH) and to a lesser extent with Alzheimer's disease pathology or recurrent stroke.

3. Post-stroke dementia is associated with higher mortality rates (from dementia itself or stroke-related mortality, more severe vascular disease and complications, less well-treated, poorer compliance to treatment), higher stroke recurrence and more impaired and dependent in activities of daily living.

4. The neurodegeneration profiles for South-East Asian populations might be different from Western populations with a study from the National Neuroscience Institute, Singapore showing that two-thirds (55.9 %) of the local population tested negative for Amyloid-β in cerebrospinal fluids (CSF). Notably, among these Amyloid negative cohorts, 40% had cerebrovascular diseases.

5. There is a higher prevalence of white matter lesions (WML) among South-East Asians.

6. Hypertension, hyperlipidemia, diabetes mellitus, smoking, higher body mass index (BMI) and carotid artery stenosis were significant risk factors for WML.

Goals

1. Better understanding of the underlying pathophysiology of post-stroke neurocognitive disorder and dementia in general.

2. Early detection of mild cognitive impairment (MCI) to prevent progression to dementia.

3. Timely initiation of pharmacological and non-pharmacological interventions.

Specific interventions: (ESO White Paper on cognitive impairment and cerebrovascular disease/ESO-EAN joint guidelines on post-stroke cognitive impairment)

Interventions	Rationale
Early symptoms recognition from clinical profile	Three essential domains: 1. Cognition (changes in vocabulary/grammar, errors at work) 2. Mood and behaviour (decreased motivation, emotional dysregulation, impulse control, social inappropriateness) 3. Physical changes (slowness of gait, cautious gait, reduced grip strength).
Screening tools	1. Brief cognitive screening at the acute stroke onset should be performed as part of the neurological examination and contributes to the diagnosis of the acute condition in the emergency room; in the stroke unit, this can be complemented with language or hemineglect tests to facilitate early rehabilitation. 2. Screening of cognition using MMSE can be considered in

	acute and post-acute stroke settings i.e. 3 to 6 months post-stroke. 3. Screening of cognition using the MoCA can be considered in post-acute stroke settings. 4. Initial full neuropsychological evaluation should only be conducted after some stabilisation was achieved (possibly as late as 6 months after a severe stroke).
CSF/Blood-based biomarkers	1. No specific laboratory analysis or blood or cerebrospinal fluid (CSF) biomarker is available yet for determining the exact vascular injury responsible for CI due to CVD. 2. In patients with small vessel disease (SVD), CSF studies may help in differentiating inflammatory myelin disorders or exclude vasculitis. CSF protein examination can provide evidence of blood-brain barrier disruption (increased CSF albumin to blood albumin ratio). 3. Analysis of CSF markers of cortical neuronal degeneration and amyloid pathology may help in detecting mixed aetiologies (eg AD is associated with reduced amyloid β1-42; CAA is associated with increased phosphorylated-tau but lower amyloid β1-42).
Brain imaging	1. Brain MRI can be considered the gold standard for diagnosis of CI due to CVD. 2. Baseline white matter hyperintensities (WMH) and lacunes (cavitated lesions) have been identified as independent

	predictors of CI in SVD, not necessarily preceded by a history of stroke. 3. Infarct volume and location, in combination with WMH, microbleeds and atrophy (globally and medial temporal lobe), maybe the most important neuroimaging predictors of PSCI. 4. The predictors of minor and major CI after ischemic stroke and after intracerebral haemorrhage appear to be largely similar, with haemorrhagic stroke associated with an increased risk of PSCI compared with ischemic stroke.

Prevention in patients with CI due to CVD	1. Comprehensive vascular risk factor management including blood pressure reduction, antithrombotic and statin is warranted following stroke even though the cognitive benefits are unclear. 2. Lifestyle modifications (obesity, physical inactivity, smoking, alcohol) should be used in adjunct with other interventions. 3. Pharmacological treatment of vascular risk factors should be applied to mild-to-moderate dementia patients. For patients with severe dementia and anticipated short life expectancy, the risk-benefit ratio of managing vascular risks is less clear.

Treatment to improve cognition in patients with CI due to CVD	1. Cholinesterase inhibitors (donepezil, rivastigmine, galantamine) and N-methyl-d-aspartate receptor antagonists (memantine) may improve cognition in CI due to CVD but did not improve behaviour or functional status. 2. The effect of these drugs is minimal in predominantly vascular CI. 3. The use of cholinesterase inhibitors and memantine might be considered in patients with CI due to CVD on a case-by-case basis where there is coexistent AD or other neurodegenerative processes, depending on the drug's authorization in respective countries, the individual tolerance of the treatment and the perceived benefit during follow-up. 4. Nimodipine, piracetam, huperzine A, cytidine di-phosphocholine and vinpocetine have no significant effect in improving CI due to CVD. 5. Others like dl-3-n-butylphthalide, ginkgo biloba extract, cerebrolysin, and actogevin have shown a limited benefit.

STROKE REHABILITATION

Reviewer: Norhayati Hussein

Stroke rehabilitation is a goal-oriented and time-based process of assisting an individual with stroke to return to an optimal level of function, and resume activity and participation within the limits of the persisting stroke impairment. Rehabilitation approaches include restoration (repairing the bodily function), compensation (an increasing function without changing the impairment), environmental modification (increasing activity and participation), prevention of complications (e.g. recurrent stroke, shoulder pain) and maintenance (i.e. prevention of deterioration). Stroke rehabilitation occurs throughout the stroke continuum of care from the acute phase to the community. The stroke patients' needs, priorities and goals for rehabilitation vary according to the trajectory or stage of recovery.

Goals:

1. Deliver high-quality, accessible, timely, appropriate stroke rehabilitation to all clinically indicated stroke survivors.
2. Initiate early post-stroke rehabilitation to enable a patient to reach an optimal functional level, independence, and quality of life.

Best Practice Recommendations

Components	Recommendations
Initiation of stroke rehabilitation in the	1. All stroke patients should be offered early access to rehabilitation and referred to the rehabilitation team as soon as possible after

acute phase (1-7 days)* *Definition from Stroke Recovery and Rehabilitation Roundtable Taskforce	admission. 2. Appropriate early stroke rehabilitation should be initiated in the acute medical ward. Early rehabilitation focuses on regaining basic functions and minimizing complications and often of lesser intensity. 3. In the subacute phase, stroke rehabilitation progressively escalates to more intensive interventions depending on the stroke patient's factors (medical stability, severity of impairment, rehab readiness eg cognition level, willingness to participate in rehabilitation), resource availability and logistics arrangement.
Stroke interdisciplinary rehabilitation team	1. Stroke patients are best managed in a stroke rehabilitation unit by a specialized rehabilitation team with a special interest in stroke. The team is ideally led by a rehabilitation physician and comprise rehabilitation nurses, physiotherapist, occupational therapist, speech therapist, with input from a counsellor, clinical psychologist, dietician, pharmacist and social welfare officer. 2. The stroke rehabilitation team members should meet regularly to discuss the assessment of new patients, review patient management and goals, and plan for post-discharge support.
Standardized and early assessment	1. All post-stroke patients should undergo early screening and assessments using standardized and validated screening and assessment tools to determine the post-stroke impairments activity limitation and restriction in participation, as outlined in the International Classification of Functioning, Disability, and Health (ICF) Model.

	2. The choice of screening tools and assessment tools should be made based on the tools' validity, reliability and availability in a stroke population to guide clinical decision-making, and perform goal-setting and discharge planning.
Management of Post-Stroke Complications & Secondary Prevention	1. Appropriate management of post-stroke complications must be managed accordingly. The commonly encountered complications include (but are not limited to): a. Infection e.g. aspiration pneumonia, UTI b. Incontinence of bowel and bladder c. Integumentary complications e.g. pressure injury d. Gastrointestinal complications e.g. GI bleeding, constipation e. Nutritional and hydration issues f. Vascular complications e.g. thromboembolism g. Musculoskeletal complications e.g. hypertonia with spasticity (refer to spasticity section), hemiplegic shoulder pain, contractures h. Mood impairment e.g. post-stroke depression, anxiety i. Sleep cycle disturbance j. Post-stroke seizures 2. Appropriate stroke secondary prevention measures must be actively instituted and reinforced during the rehabilitation phase.
Post-Stroke Spasticity (PSS)	1. The presence of spasticity should be identified as early as possible by performing clinical examination and assessment using a standardized scale such as the Modified Ashworth Scale (MAS) or Tardieu Scale.

	2. Comprehensive spasticity management must include identifying and managing spasticity-related issues which lead to difficulty in performing activities of daily living and reduction in quality of life (e.g. pain, impaired body image etc) 3. Post-stroke spasticity management options include: a. Non-pharmacological approaches: therapeutic exercises, electrical stimulation, orthotics, hydrotherapy. b. Pharmacological approaches: oral anti-spasmodic for segmental and generalized spasticity, intramuscular botulinum toxin-A injection for focal spasticity, intrathecal Baclofen Therapy (ITB) for severe segmental or generalized spasticity.
Rehabilitation Interventions in the Subacute Phase* (Early Subacute: 7 days to 3 months * Late subacute: 3-6 months*) Definition from Stroke Recovery and Rehabilitation Roundtable Taskforce	1. In the subacute phase, the key approaches predominantly incorporate neuroplasticity mechanisms in the brain and are more restorative. The stroke rehabilitation interventions are multimodal, task-specific and of higher intensity. The combination of multimodal interventions is specifically planned based on the post-stroke impairments and patient-centred rehabilitation goals, best in an enriched environment to enhance recovery. 2. Common interventions for motor rehabilitation comprise of (but are not limited to): a. Mirror-based therapy b. Mental imagery c. Constraint-induced movement therapy d. Electromechanical and robotic-assisted walking

	e. Functional electrical stimulation (FES) f. Non-invasive brain stimulation (transcranial direct current stimulation (TdCS) or repetitive transcranial magnetic stimulation (rTMS) 3. Interventions for other post-stroke impairments (eg aphasia, neglect, visual field deficits etc) are planned according to the specific needs of the patient.
Caregiver Training & Education	1. Relevant members of the stroke rehabilitation team should provide specific and tailored training for caregivers/families before discharge. This should include training in personal care techniques, communication strategies, physical handling techniques, safe swallowing and appropriate dietary modifications, ongoing prevention and other specific stroke-related problems, in addition to management of behaviour and psychosocial issues. 2. The educational training of family/caregivers should also address the nature and clinical manifestations of stroke, risk factors management, potential post-stroke complications, (e.g. malnutrition, swallowing difficulties, pressure injury and aspiration pneumonia), as well as additional information on health resources available and community support. 3. The educational content and information may need to be adjusted along the stroke recovery trajectory as the patient's needs are likely to evolve with time. Education and information can be offered throughout the stroke continuum of care to include acute care, secondary

	prevention, rehabilitation, community reintegration including work vocation.
Community Long-Term Follow-Up	1. Stroke patients living in the community should have regular follow-ups by respective teams in the community setting to assess recovery, prevent deterioration, maximize functional and psychosocial outcomes, and improve quality of life. 2. Monitoring, re-evaluation and re-entry points to rehabilitation shall be made available throughout the stroke care continuum in the community.

REORGANIZATION OF STROKE NETWORK

Reviewer: Irene Looi, Wan Chung Law

Issues

1. 41,000 acute stroke patients were admitted to MOH hospitals every year and the number is increasing in trend. 11% of patients died during hospital admission while 55% were left permanently disabled.

2. In Malaysia, < 5% of AIS patients receive IVT whereas <2% receive EVT.

3. ASU/wards are not widely available throughout MOH hospitals.

4. Lack of stroke physicians, infrastructure and support teams in rural and remote areas.

5. Potential obstacles (legislation issues) in credentialing and privileging non-neurologists/non-stroke physicians to render thrombolysis.

Goals

1. To reduce stroke-related morbidities and mortalities in Malaysia.

2. To strengthen the national stroke care service which encompasses the entire chain of care from primary prevention to life post-stroke.

2. To focus resource allocation on the following:

a. Ensuring rapid access to all stroke services including emergency transport with the support of appropriate communication technologies, essential brain imaging, and IVT/MT service.

b. Developing acute stroke care units and facilities in all MOH hospitals with specialists.

c. Ensuring access to healthcare workers most skilled in stroke care.

d. To build up a multidisciplinary stroke team in all major hospitals to improve the post-stroke recovery of all patients.

e. Ensure all eligible individuals are given the best standard of treatment regardless of financial status.

Specific Interventions

1. Organisational strategies should be developed at all levels including the local level (urban, rural, and remote), taking into consideration resource availability and geographical constraints.

2. Joints efforts from the following stakeholders are essential in ensuring the smooth delivery of national stroke care service:

Stakeholders	Responsibilities
Emergency medical services (EMS)	1. Improve EMS prenotification and raise awareness on the benefits of prenotification to allow more patients to undergo timely evaluation, shorten onset-to–needle and door-to–needle times, and thus more eligible acute ischemic stroke patients being treated with tPA. 2. This will include organised stroke teams, written protocols for acute triage and patient flow, an **organised stroke code system** to facilitate rapid communication between all stroke team members, computed tomography (CT) or magnetic resonance imaging (MRI) scanner clearance before patient's arrival, rapid access to the thrombolytic drug in the

	Emergency Department, and collaboration between Emergency Medicine, Neurology and Radiology. 3. Provide adequate training for EMS staff in stroke screening tools for timely identification of ischemic stroke together with hospital prenotification. 4. Use of **validated metrics** e.g. Balance, Eyes, Face, Arm Speech Test (BEFAST) and NIHSS score to allow swift identification of acute stroke and prompt initiation of treatment for eligible individuals.
Acute stroke ready hospital	1. To establish more acute stroke-ready hospitals among **district hospitals with specialists** to cater for the increasing number of stroke patients. 2. To **decentralise stroke care** to **district hospitals** with specialists to reduce median onset-to-needle times and improve overall functional outcomes. 3. **Ensure prompt treatment and referral to CSC** for patients who may be eligible for EVT to reduce median onset to reperfusion time. 4. Adoption of **telemedicine** to provide evidence-based acute stroke treatment. 5. Participation in **certification** and **stroke audit programmes** to ensure continuous delivery of high-quality care.
Stroke centre	1. Act as a **coordinating body** of the **entire chain** of care that

	covers pre-hospital service, diagnostic imaging, quality inpatient care with access to neurosurgical intervention and ICU back-up, post-stroke rehabilitation and secondary prevention. 2. Provision of **stroke services** for the **population** of its catchment area and serve as a **referral centre** for **peripheral hospitals**. (Hub-and-spoke model) 3. Set up a **specific task force** to improve inpatient bed management. 4. Setting up dedicated stroke units which offer a multidisciplinary treatment of strokes by highly qualified stroke teams in addressing acute treatment, early mobilisation and rehabilitation as well as secondary prevention. It should be equipped with defined infrastructure equipment and well-organised standard operating procedures. 5. Early supported **discharge** and **community rehabilitation** for patients with mild-moderate stroke to reduce the length of hospital stays.
State Stroke Champion	1. To lead the **stroke service** in the **respective state** in the areas related to: a. **Clinical management** (Hyperacute stroke, acute stroke and stroke rehabilitation) b. **Resource management** (financial, equipment and human resource allocations)

	c. **Training of stroke care personnel** 2. Liaise with the **state health department** in **planning** and ensuring the objectives of national stroke action plans are achieved at the state level. 3. Work with the state health department in ensuring that a stroke management team with committee members are established at the hospital level and stroke service is provided by MOH guidelines. 4. To supervise the **training** of stroke care personnel at every health facility in the state. 5. Ensure all **stroke units** and **stroke services** undergo regular **certifications** or **auditing processes** for **quality improvement.** 6. Ensure that the **National Stroke Registry** is regularly updated at the state level. 7. **Resolve issues** on stroke management in the state together with state health department / clinical experts.
Stroke Council MSN (Malaysian Society of Neurosciences)	1. Ensure the provision of stroke thrombolysis is following medical ethics and evidence-based guidelines. 2. Act as **coordinator** or **governance body** for the provision of **stroke service** among **stroke physicians, geriatricians, emergency physicians and neuro-radiologists**. 3. **Training** of stroke care personnel

	4. To establish a **proper stroke service credentialing and privileging pathway** (stroke training modules, logbook, preceptorship in stroke centre) for physicians with a special interest in stroke. 5. **Identify** or establish **key national institutions** or organisations that promote the **training** and **education** of **stroke physicians.**
Ministry of Health Malaysia	1. Increase **financial allocation** for **acute stroke treatment**. 2. Increase **asset allocation** to establish **acute stroke units** that are equipped with modern medical **technologies** and **facilities** in major hospitals. 3. To collaborate with **Stroke Council MSN and NGO, besides having PPP (Public-Private-Partnership)** to foster better-coordinated stroke services across the country 4. To support the development of **telemedicine systems** for acute stroke, rehabilitation and long-term care 5. To organise evidence-based **media campaigns** to promote public awareness of stroke symptoms, early treatment and benefits of a healthy lifestyle. 6. Supporting self-management and peer support for stroke survivors and their families, by backing **stroke support organisations** such as NASAM.

	7. To support basic and clinical **stroke research** which can improve the management and treatment of acute ischemic stroke.
SOSCO / NGOs / Charity Organisation/ Insurance company	To work closely with various healthcare stakeholders to support individuals who are **financially disabled** in stroke emergency settings.

THE ROLE OF SOCIAL SECURITY ORGANIZATION (SOSCO)IN STROKE CARE

Reviewer: Hafez Hussain, Parathythasan Rajaandra

Goals:

1. To provide financial assistance to SOSCO's insured individuals and make healthcare more affordable for all eligible individuals.
2. Provision of good quality and intensive rehabilitation to SOSCO's contributors in a comprehensive rehabilitation centre and ensure that they recover physically, vocationally and psychologically before finally returning to work
3. Expansion of service to other states especially East Malaysia other than the current Tun Razak Rehabilitation Centre (TRRC) and four others which are located at Tanjung Pelepas in Johor, Kuala Terengganu, Ara Damansara in Selangor, and Quill City Mall in Kuala Lumpur.

Specific Interventions:

Interventions	Rationale
Disability management	Implementation of a rehabilitation plan that focuses on providing a comprehensive and customised rehabilitation plan according to an individual's functional level and capability.
Medical rehabilitation	1. Preliminary patient assessment to be carried out based on a biopsychosocial model that focuses on physical functioning factors, mobilisation levels, physiological and

	psychological conditions as well as environmental factors and the individual's goal to recover or return to work. 2. Provision of rehabilitation services which include physiotherapy, occupational therapy, clinical psychology, speech therapy, audiology, optometry and diet therapy.
Neuro-robotics and Cybernetics rehabilitation	1. Latest technologies like robotic suits improve, support and enhance the wearer's limb mobility via cybernic technology that combines interactions between man, machine and information to speed up the recovery of patients. 2. For example, Social Security Organisation (SOCSO) in collaboration with Cyberdyne Inc. Japan has successfully established the first Neuro-Robotics Rehabilitation & Cybernetics Centre in Malaysia at SOCSO Tun Razak Rehabilitation Centre, Melaka. This centre is equipped with Hybrid Assistive Limb (HAL) Robot Suit, the latest neurorobotic technology equipment from Cyberdyne Inc. Japan assists people with paralysis or weakening limbs due to injuries or disorders to the central nervous system to regain the ability to walk.
Vocational rehabilitation	Ensure that patients are equipped with necessary skills to live independently and return to work.
Facilities & accommodation	Rehabilitation centre which also provides comfortable accommodation/wards, sports arena, dispensary, cafe and

	self-ordering food system.
Digital platform	Promote the use of the PERKESO INSPIRE DR Portal among healthcare providers to facilitate medical reimbursement for eligible patients.
Neurosurgery team	Offer vagus nerve stimulation under the support of neurosurgery team and to enhance plasticity and support recovery of limb function after stroke.
University hospitals	Collaboration with university hospitals in: a. Stroke prevention programme, eg the SOSCO-UPM "Early Stroke Disability Prevention Programme " b. Research related to rehabilitation engineering (eg Universiti Malaysia Perlis, Universiti Tun Hussein Onn Malaysia)

TELEMEDICINE IN LONG TERM STROKE CARE

Reviewer: Wan Chung Law

Challenges

1. Medico-legal liabilities (lack of safeguards for data privacy).

2. Technological and infrastructure interoperability, and digital literacy.

3. Cost of implementation.

4. Issues with reimbursement and subsidies.

Goals:

1. Providing care which is patient-centred, cost-effective, convenient and yields greater productivity.

2. Quick access to better and equitable neurological care.

3. Reduce risk of stroke-related complications and disabilities due to timely decisions on patient management.

4. Minimise patient transfer expenses and risks.

5. Improve diagnostic accuracy in emergency care.

Specific interventions:

1. Identify problems that are feasible to be used for telemedicine, i.e. symptoms that are persistent or worrisome, not life-threatening but need to be addressed.

a. Stroke risk factors control

b. Acute stroke or non-stroke-related problems (pressure sore/diarrhoea/constipation)

c. Progress of stroke rehabilitation

2. Points to be considered when choosing candidates for telemedicine:

a. Social background (lack of caregiver support, logistic and finance)

b. Mental health issues of both patient and caregivers

c. Safety precautions (aim for social distancing during the pandemic)

3. Ensure prerequisites for stroke telecare are met, i.e.

a. Patient and/or caregivers consented to virtual sessions and recording

b. Patient and/or caregivers are digitally literate

c. Availability of home monitoring device (Blood pressure pump, glucometer etc)

d. Achievable objectives for each session (summarize instructions and goals)

e. Supports are provided to patients and/or caregivers in case of emergency (safety netting)

f. List of prescriptions, blood results (if any)

g. Appropriate settings i.e. quiet location with good lighting and strong wifi's signal

4. Adherence to criteria for long-term shared care follow-up (adapted from Integrated Care Pathway for Poststroke iCAPPS):

a. Age ≥ 40 years old at the onset of stroke

b. No concurrent heart disease

c. Coronary artery stenosis if present, lumen patency ≥ 50%

d. Normal renal function

e. Well-controlled stroke risk factors

Areas of improvements

1. Regular audit of telestroke service by maintaining a registry of patients contacted for stroke telecare, considering the storage of telecare consultations for reference and recording the outcome of consultations.

2. Using patient and caregivers' reported outcome/ satisfaction with stroke telecare to

guide service improvement strategies.

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